INDEVUS PHARMACEUTICALS INC
Form POS AM
March 31, 2004
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As filed with the Securities and Exchange Commission, on March 31, 2004

Registration Number 333-109263

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Post-Effective Amendment No. 3

to

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

Indevus Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**04-3047911**
(State or other jurisdiction of incorporation)	**(I.R.S. Employer Identification No.)**

One Ledgemont Center

99 Hayden Avenue

Lexington, MA 02421-7966

(781) 861-8444

(Address, including zip code, and telephone number, including area code of registrant s principal executive offices)

Glenn L. Cooper, M.D., President, Chief Executive Officer and Chairman

One Ledgemont Center

99 Hayden Avenue

Lexington, MA 02421-7966

(781) 861-8444

(Name, address, including zip code and telephone number, including area code, of agent for service)

Josef B. Volman, Esq.

Burns & Levinson LLP

125 Summer Street

Boston, MA 02110-1624

(617) 345-3000

Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the Securities Act) other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. ¨

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CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered	Proposed maximum offering price per Share	Proposed maximum aggregate offering price	Amount of registration fee(3)
6.25% Convertible Senior Notes due July 15, 2008	$72,000,000	100%	$72,000,000	$5,825
Common Stock, $.001 Par Value per share	10,817,309(1) 59,686	n/a $5.565(2)	n/a $332,153	n/a $27

(1) This number represents the number of shares of common stock that are initially issuable upon conversion of the 6.25% Convertible Senior Notes due July 15, 2008 registered hereby. For purposes of estimating the number of shares of common stock to be included in the registration statement upon conversion of the notes, Indevus Pharmaceuticals, Inc. calculated the number of shares issuable upon conversion of the notes based on a conversion rate of 150.2404 shares per $1,000 principal amount of the notes. In addition to the shares set forth in the table, the amount to be registered includes an indeterminate number of shares of Common Stock issuable upon conversion of the notes, by means of adjustment to the conversion price applicable thereto. Pursuant to Rule 457(i) under the Securities Act of 1933, there is no filing fee with respect to the shares of common stock issuable upon conversion of the exercise of the conversion privilege.

(2) Estimated in accordance with Rule 457(c) of the Securities Act solely for the purpose of computing the amount of registration fee based on the average of the high and low prices of the registrant s Common Stock as reported on The Nasdaq National Market on September 26, 2003.

(3) Calculated in accordance with Rule 457(o) of the Securities Act and previously paid.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(A) OF THE SECURITIES ACT OF 1933, AS AMENDED OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(A), MAY DETERMINE.

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Registration No. 333-109263

Indevus Pharmaceuticals, Inc.

6.25% Convertible Senior Notes Due July 15, 2008

and

Shares of Common Stock Issuable Upon Conversion of the Notes

This prospectus relates to $72,000,000 in aggregate principal amount of 6.25% Convertible Senior Notes due July 15, 2008 of Indevus Pharmaceuticals, Inc. and 10,817,309 shares of common stock of Indevus Pharmaceuticals, Inc., which are initially issuable upon conversion of the notes, plus an indeterminate number of shares as may become issuable upon conversion as a result of adjustments to the conversion rate. The notes were originally issued and sold by Indevus Pharmaceuticals, Inc. in a private placement on July 16, 2003. This prospectus will be used by selling securityholders to resell their notes and the common stock issuable upon conversion of the notes.

We will not receive any proceeds from the sale of the notes or shares of common stock issuable upon conversion of the notes by any of the selling securityholders. Holders of the notes or the shares of our common stock issuable upon conversion of the notes may offer the notes or the common stock for sale at any time at market prices prevailing at the time of sale or at privately negotiated prices. The selling holders may sell the notes or the common stock directly to purchasers or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions.

Interest on the notes is payable on January 15 and July 15 of each year, commencing on January 15, 2004. The notes are convertible into our common stock at any time prior to the close of business on the business day prior to the maturity date of the notes, unless previously redeemed or repurchased, into 150.2404 shares of our common stock per $1,000 principal amount of notes, subject to adjustment in certain circumstances. This rate results in an initial conversion price of approximately $6.656 per share.

On or after July 20, 2006, we may at our option redeem the notes, in whole or in part, at the redemption prices described in this prospectus, plus any accrued and unpaid interest to the redemption date; provided that the closing price of our common stock has exceeded 150% of the conversion price then in effect for at least 20 trading days within a period of 30 consecutive trading days ending on the date of mailing of the provisional redemption notice to holders. In the event of a change in control (as defined in this prospectus) of Indevus Pharmaceuticals, Inc., each holder of notes may require us to repurchase the notes at 100% of the principal amount of the notes plus accrued and unpaid interest.

Our common stock is listed on the Nasdaq Stock Market under the symbol IDEV. The closing sales price of the common stock on March 29, 2004 was $6.22 per share.

The notes originally issued in the private placement are eligible for trading on the PORTAL Market of the National Association of Securities Dealers, Inc. However, notes sold pursuant to this prospectus will no longer be eligible for trading on the PORTAL Market. We do not intend to list the notes on any national securities exchange.

Indevus Pharmaceuticals, Inc. is a Delaware corporation. Our principal office is at One Ledgemont Center, 99 Hayden Avenue, Lexington, Massachusetts 02421-7966 and our main telephone number is (781) 861-8444.

Investing in the notes or our common stock involves a high degree of risk. You should carefully consider the risk factors beginning on page 5 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or the accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this Prospectus is March 31, 2004

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IMPORTANT NOTICE TO READERS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf registration process, the selling securityholders may, from time to time, offer notes or shares of our common stock owned by them. Each time the selling securityholders offer notes or common stock under this prospectus, they will provide a copy of this prospectus and, if applicable, a copy of a prospectus supplement. You should read both this prospectus and, if applicable, any prospectus supplement together with the information incorporated by reference in this prospectus. See Where You Can Find More Information and Incorporation by Reference for more information.

You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized anyone else to provide you with different information. If anyone provides you with different information, you should not rely on it. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus or any document incorporated by reference in this prospectus is accurate only as of the date on the front cover of the applicable document or as specifically indicated in the document. Our business, financial condition, results of operations and prospects may have changed since that date.

Unless otherwise indicated, in this prospectus, Indevus, the Company, we, us and our refer to Indevus Pharmaceuticals, Inc. and its subsidiar

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SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

Statements in this prospectus, and the documents incorporated by reference into this prospectus, that are not statements or descriptions of historical facts are forward-looking statements under Section 21E of the Securities Exchange Act of 1934, as amended, (the Exchange Act) and the Private Securities Litigation Reform Act of 1995 and are subject to numerous risks and uncertainties. These and other forward-looking statements made by us in reports that we file with the SEC, press releases, and public statements of our officers, corporate spokespersons or our representatives are based on a number of assumptions and relate to, without limitation: our ability to successfully develop, obtain regulatory approval for and commercialize any products, including trospium; our ability to enter into corporate collaborations or to obtain sufficient additional capital to fund operations; and the Redux-related litigation. The words believe, expect, anticipate, intend, plan, estimate or othe expressions which predict or indicate future events and trends and do not relate to historical matters identify forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements as they involve risks and uncertainties and such forward-looking statements may turn out to be wrong. Actual results could differ materially from those currently anticipated due to a number of factors, including those set forth under Risk Factors and elsewhere in, or incorporated by reference into, this prospectus. These factors include, but are not limited to: dependence on the success of trospium; the early stage of products under development; uncertainties relating to clinical trials, regulatory approval and commercialization of our products, including trospium; risks associated with contractual agreements; dependence on third parties for manufacturing and marketing; competition; need for additional funds and corporate partners, including for the commercialization of trospium and for the development of our other product candidates; failure to acquire and develop additional product candidates; history of operating losses and expectation of future losses; product liability and insurance uncertainties; risks relating to the Redux-related litigation; limited patent and proprietary rights; dependence on market exclusivity; valuation of our Common Stock; risks related to repayment of debts; risks related to increased leverage; and other risks. The forward-looking statements represent our judgment and expectations as of the date of this prospectus. Except as may otherwise be required by applicable securities laws, we assume no obligation to update any such forward-looking statements.

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PROSPECTUS SUMMARY

This summary provides an overview of selected information and does not contain all the information you should consider. Before making an investment decision, you should carefully read the entire prospectus, including the section entitled Risk Factors and the documents incorporated by reference into this prospectus.

Indevus Pharmaceuticals, Inc.

Indevus is a biopharmaceutical company engaged in the development and commercialization of a diversified portfolio of product candidates, including multiple compounds in late-stage clinical development. We currently have rights to six compounds in development: trospium for overactive bladder, pagoclone for panic and generalized anxiety disorders, IP 751 for pain and inflammatory disorders, PRO 2000 for the prevention of infection by HIV and other sexually-transmitted pathogens, aminocandin for treatment of systemic fungal infections, and citicoline for ischemic stroke.

We seek to acquire, develop and commercialize a portfolio of pharmaceutical products for a range of therapeutic indications. The key elements of our business strategy include: (1) identifying product candidates with broad applications and large, unsatisfied markets, (2) acquiring clinical and late pre-clinical stage compounds, including products with clinical data or market experience outside the United States, (3) defining strategies to take these compounds through clinical testing and to market, (4) adding value to acquired products through clinical testing and regulatory review activities, and (5) commercializing products in collaboration or combination with corporate partners in order to help ensure the timely penetration of target markets. Our strategy encompasses a range of products and therapeutic areas arising from our relationships with a diverse range of partners including biopharmaceutical, regional pharmaceutical, and multi-national pharmaceutical firms, as well as academic and government institutions. Our rights with respect to our current product candidates have been licensed from third parties.

Our lead product candidate is trospium chloride (trospium), a muscarinic receptor antagonist in development as a treatment for overactive bladder. On June 27, 2003, the U.S. Food and Drug Administration (FDA) accepted for filing our New Drug Application (NDA) for trospium. We received a letter dated February 12, 2004, from the FDA establishing a 90-day extension to the original Prescription Drug User Fee Act (PDUFA) action date of February 27, 2004, moving that date to May 28, 2004. The NDA for trospium includes data from 34 clinical studies involving over 2,800 subjects and patients, including 14 double-blind, placebo- or active-controlled studies, 12 clinical pharmacology and pharmacokinetic studies and 8 uncontrolled studies. Results from previous clinical trials and our 523-patient Phase III trial demonstrated that treatment with trospium significantly reduced the frequency of both urination and incontinence episodes in patients with overactive bladder. We also completed a study to assess the effect of trospium on the QT interval of cardiac muscle contractility which concluded that trospium has no significant effect on the QT interval. In addition, we recently completed a successful 658-patient trial designed to explore further certain attributes of trospium. Preliminary results show that the trial met all of its primary and secondary endpoints with a high degree of statistical significance, including a reduction in both micturitions (urinations) and urinary incontinence episodes among patients treated with trospium versus placebo. In addition to the twice-a-day formulation of trospium which is the subject of the filed NDA, we have entered into an agreement with Shire Laboratories, Inc. (Shire) to develop extended release, once-a-day formulations. We are currently evaluating commercial opportunities for trospium, including co-promotion and licensing arrangements, strategic combinations, and other partnering opportunities. It is estimated that more than 17 million Americans suffer from overactive bladder in the United States. According to a recent *SCRIP* Report, only 20 percent of overactive bladder patients are currently treated with pharmacotherapy. In 2002, the market for drugs to treat overactive bladder was approximately $1 billion in the United States. We have exclusive rights to develop and market trospium in the United States. Trospium is currently marketed in Europe, where it is one of the leading treatments for overactive bladder.

Pagoclone is a GABA (gamma amino butyric acid) receptor agonist for the treatment of anxiety disorders. Pagoclone is in Phase III clinical stage development for panic disorder and Phase II for generalized anxiety disorder (GAD). To date, there have been three Phase II clinical trials of pagoclone that demonstrated statistically significant efficacy, two in panic disorder and one in GAD, as well as three other clinical trials that did not

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demonstrate statistically significant efficacy. Results from these clinical trials suggest the potential of pagoclone as a novel anti-anxiety agent that is free from the sedative effects and withdrawal or rebound-anxiety symptoms seen with other anti-anxiety agents. We are pursuing new development and commercialization partnerships for pagoclone, and we are planning to initiate an additional clinical trial with pagoclone in 2004. We have exclusive, worldwide rights to develop and market pagoclone.

IP 751 is a non-psychoactive synthetic derivative of tetrahydrocannabinol (THC). Pre-clinical studies have shown that this novel anti-inflammatory and analgesic compound inhibits inflammatory cytokines, particularly interleukin 1-beta and TNF-alpha. In addition, results of a Phase II clinical trial conducted in Germany and published in the Journal of Medical Association in September 2003 showed that treatment with IP 751 significantly reduced neuropathic pain among 21 patients and was well-tolerated, without causing psychoactive adverse events. An initial Phase I clinical trial designed to assess the safety of IP 751 showed that it was well-tolerated, with no clinically significant adverse events and no evidence of psychoactive properties. An Investigational New Drug Application (IND) for IP 751 has been filed with the FDA. Additional Phase I and Phase II clinical trials are currently being planned for IP 751. We have exclusive, worldwide rights to develop and market IP 751.

PRO 2000 is a topical microbicide in development for the prevention of the sexual transmission of HIV and other sexually-transmitted diseases (STDs). Government-sponsored Phase I and Phase I/II clinical trials in both healthy and HIV-positive women have shown PRO 2000 to be well-tolerated. In February 2002, PRO 2000 was selected for a broad, five-year testing program of vaginal microbicides by an international collaboration of research groups in the United Kingdom and Africa under a grant from the United Kingdom. Department for International Development (DFID). A Phase II clinical trial in Africa, funded by the European Commission, is currently underway to assess the safety of PRO 2000. It is expected that in 2004 a National Institutes of Health (NIH)-sponsored Phase II clinical trial will begin and may extend to a Phase III clinical trial to determine its safety and efficacy in preventing male and female HIV transmission. We have exclusive, worldwide rights to develop and market PRO 2000.

Aminocandin is an echinocandin, a new class of anti-fungal compounds in development for the treatment of a broad spectrum of systemic, invasive fungal infections. Aminocandin has shown *in vitro* and *in vivo* activity against a number of candida and aspergillus fungal species. We expect aminocandin will be ready for Phase I clinical testing in early 2004 as an intravenous agent. We believe that aminocandin also has potential to be delivered orally, unlike the currently approved drugs or those under development in its class that can be delivered only intravenously. We plan to pursue technological solutions related to an oral formulation in parallel with an intravenous clinical program. We have exclusive, worldwide rights to develop and market aminocandin.

Citicoline is cytidine-5 diphosphate choline, a precursor for the biosynthesis of phosphatidylcholine, a major building block of nerve cell membranes, and has been under development as a neuroprotective treatment for ischemic stroke. We have completed three Phase III clinical trials and one Phase II/III clinical trial with citicoline in North America. We believe that these studies may indicate the effectiveness of citicoline in reducing the disability associated with ischemic stroke utilizing various outcome measures. However, only one of these trials has successfully met its primary outcome objective. Two meta-analyses of clinical trials presented at the 27th International Stroke Conference in February 2002 and a recently published analysis of pooled data from various controlled trials suggest that treatment with citicoline may reduce infarct growth after stroke and reduce rates of death or disability over the long term. We believe that additional clinical testing of citicoline is required before an NDA can be submitted. Pursuant to a new agreement with Ferrer Internacional S.A. (Ferrer) in January 2004, we have granted Ferrer exclusive rights to our patents and know-how related to citicoline and Ferrer agreed to assume all future development, manufacturing, and commercialization costs of citicoline. Indevus will receive 50% of all milestone payments made to Ferrer by a third party and royalties on net sales of the product.

In addition to our product candidates in development, we are receiving royalties under a patent we licensed to Eli Lilly & Company (Lilly) based on net sales of Sarafem in the United States. Sarafem is prescribed to treat certain conditions and symptoms associated with pre-menstrual syndrome.

Indevus Pharmaceuticals, Inc. is a Delaware corporation. Our principal office is at One Ledgemont Center, 99 Hayden Avenue, Lexington, Massachusetts 02421-7966 and our main telephone number is (781) 861-8444.

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The Offering

Securities Offered	$72 million aggregate principal amount of 6.25% Convertible Senior Notes due July 15, 2008 and 10,817,309 shares of our Common Stock, $0.01 par value per share, issuable upon conversion of the notes.
Maturity	July 15, 2008, unless earlier converted or redeemed by us at our option or repurchased by us at your option.
Interest Rate	The notes bear interest at 6.25% per year. Interest will be payable semiannually in arrears on January 15 and July 15 of each year, commencing January 15, 2004. The initial interest payment will include accrued interest from July 16, 2003.
Conversion Rights	Holders may convert their notes into our common stock at any time prior to the close of business on the business day prior to the maturity date of the notes, unless previously redeemed or repurchased, at a conversion price of $6.656 per share (equal to a conversion rate of approximately 150.2404 shares per $1,000 principal amount of notes), subject to adjustment as described under Description of Notes Conversion Rights.
Provisional Redemption of Notes at Our Option	We may redeem all or a portion of the notes for cash at any time on or after July 20, 2006, at 100% of their principal amount plus accrued and unpaid interest to, but excluding, the redemption date; provided, that the current market value (as defined in this prospectus) of our common stock equals or exceeds 150% of the conversion price then in effect for at least 20 trading days in any consecutive 30 trading day period ending on the date we mail the provisional redemption notice to holders. We will therefore be required to make at least six interest payments on the notes before being able to redeem any notes. See Description of Notes Provisional Redemption by Indevus.
Sinking Fund	None.
Change of Control Put Right	Upon a change of control of Indevus, each holder may require us to repurchase for cash all or a portion of its notes at a repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest thereon to, but excluding, the repurchase date. See Description of Notes Repurchase at Option of Holders Upon a Change of Control.
Events of Default	If there is an event of default on the notes, the principal amount of the notes plus accrued and unpaid interest to the date of acceleration may be declared immediately due and payable subject to certain conditions set forth in the indenture. These amounts automatically become due and payable in the case of certain types of bankruptcy or insolvency events of default involving Indevus.
Use of Proceeds	All of the notes and the shares of our common stock issuable upon conversion of the notes are being sold by the selling securityholders or

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	by their pledgees, donees, transferees or other successors in interest. We will not receive any proceeds from the sale of the notes or the shares of our common stock issuable upon conversion of the notes.
DTC Eligibility	The notes will be issued in book-entry form and will be represented by one or more permanent global certificates deposited with a custodian for and registered in the name of a nominee of The Depository Trust Company in New York, New York. Beneficial interests in the notes will be shown on, and transfers will be effected only through, records maintained by DTC and its direct and indirect participants and any such interest may not be exchanged for definitive securities, except in limited circumstances. See Description of Notes Form, Denomination and Registration.
Registration Rights	Pursuant to a registration rights agreement, we have filed a shelf registration statement, of which this prospectus is part, with respect to the notes and the common stock issuable upon conversion of the notes. See Description of the Notes Registration Rights.
Indenture and Trustee	We have issued the notes under an Indenture, dated as of July 16, 2003, between The Bank of New York, as trustee, and us.
Trading Market	The notes originally issued in the private placement are eligible for trading on the PORTAL market of The Nasdaq Stock Market. However, notes sold pursuant to this prospectus will no longer be eligible for trading on the PORTAL Market. We do not intend to include the notes in any other automated interdealer quotation system or list the notes on any securities exchange. Our common stock is traded on the Nasdaq Stock Market under the symbol IDEV.

Ratio Of Earnings To Fixed Charges

The following table shows the ratio of earnings to fixed charges for Indevus for the periods indicated. In calculating the ratio of earnings to fixed charges, earnings consist of income before income taxes and cumulative effect of accounting change and fixed charges.

	Fiscal Years Ended September 30,					Three Months Ended	
	1999	2000	2001	2002	2003	December 31, 2002	December 31, 2003
Ratio of earnings to fixed charges		70.3x	31.9x				

(1) The ratio of earnings to fixed charges is not presented for the fiscal years ended September 30, 1999, 2002 and 2003 and the three month periods ended December 31, 2002 and 2003 because in each such period fixed charges exceeded earnings due to our operating losses incurred in these periods. Fixed charges exceeded earnings by $38,863,000, $17,621,000 and $31,847,000 for the fiscal years ended September 30, 1999, 2002 and 2003, respectively and by $5,440,000 and $13,325,000 for the three month periods ended December 31, 2002 and 2003, respectively. We calculated our ratio of earnings to fixed charges by dividing (A) (i) income from continuing operations, plus (ii) one third of rent expense which is deemed representative of an interest factor, plus (iii) interest expense, plus (iv) equity in net income (loss) of unconsolidated subsidiary, by (B) fixed charges consisting of (i) one third of rent expense which is deemed representative of an interest factor, (ii) interest expense, and (iii) dividends on preferred stock.

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RISK FACTORS

Before purchasing the notes, you should carefully consider the following risk factors in conjunction with the other information contained in this prospectus, including the financial statements in our Annual Report on Form 10-K for the year ended September 30, 2003. These factors, among others, could cause actual results to differ materially from those currently anticipated and contained in forward-looking statements made in this prospectus and presented elsewhere by our management from time to time. See Special Note Regarding Forward Looking Statements.

Risks Related to Our Business

We will depend on the success of trospium.

Our future success will depend in large part on the success of trospium. There are many risks associated with the successful approval, manufacturing and commercialization of trospium.

Regulatory risks

On April 28, 2003, we submitted an NDA for trospium with the FDA and on June 27, 2003 the FDA accepted the NDA for filing. We received a letter dated February 12, 2004 from the FDA establishing a 90-day extension to the original Prescription Drug User Fee Act (PDUFA) action date of February 27, 2004, moving that date to May 28, 2004. We would be materially adversely affected if we are unable to obtain FDA approval for trospium or if the FDA should require additional testing prior to FDA approval. In addition, the FDA may impose post-marketing or other regulatory requirements after approval, which could have an adverse affect on the commercialization of trospium. In addition, although trospium has thus far demonstrated an acceptable safety profile in clinical trials, there can be no assurance that the safety profile of the drug would not change when taken in future trials or by a larger population of users.

Risks related to the commercialization of trospium

Even if we receive FDA approval for trospium, we do not have the necessary sales and marketing capability or financial resources to market trospium. Although we have been in discussions regarding a variety of strategic transactions and collaborative arrangements, we would be materially adversely affected if we were unable to find a corporate partner on acceptable terms or at all. We will be highly dependent on any strategic or collaborative partner for the commercialization of trospium and we, in combination or collaboration with any partner, may not be successful in commercializing trospium. We would be materially adversely affected if trospium did not achieve or maintain market acceptance. We will also be dependent on Madaus AG (Madaus), the licensor of trospium to us and the current manufacturer of trospium, to manufacture trospium for us. We are working with Madaus to achieve compliance with FDA requirements for manufacturers of drugs sold in the United States. If Madaus were unable to achieve or maintain compliance, we would need to seek alternative sources of supply, which could delay the commercialization or create disruptions in the supply of trospium. Our pending NDA relates to an immediate release, twice-a-day formulation of trospium. We have entered into an agreement with Shire to develop extended release, once-a-day formulations of trospium. If efforts to develop a once-a-day formulation are unsuccessful, we will rely on sales solely from the twice-a-day formulation which may suffer from generic penetration after the expiration of any market exclusivity period and from competition with once-a-day and other formulations of competing

products.

Risks related to competition in the overactive bladder market

Competition in the overactive bladder market is intense and expected to increase. Trospium may not compete successfully with current drug therapies for overactive bladder or with new drugs which may reach the market in the future. Trospium will compete with drugs from large, multinational companies who have

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substantially greater marketing and financial resources and experience than us. Trospium will compete with other therapies for overactive bladder, including anticholinergics currently on the market. In addition, antimuscarinic and antispasmodics for overactive bladder are the subject of testing or commercialization efforts by other companies, including certain treatments for which NDAs have already been filed. No assurance can be given that trospium, if approved by the FDA, will be able to compete successfully against existing or new products. In addition, our ability to compete with existing or new products will also be affected by labeling that may be approved by the FDA.

Lack of Patent Protection

Our license for trospium does not include any patents that we expect to use in commercializing the product for overactive bladder. Assuming FDA approval for trospium is obtained, our ability to successfully commercialize trospium in the United States will depend on the availability of market exclusivity under the Drug Price Competition and Patent Term Restoration Act of 1984, which is commonly known as the Waxman-Hatch Act, which provides protections for certain new products. Under the Waxman-Hatch Act, a company which does not have a patent on a compound may obtain five years of market exclusivity if the FDA determines such compound to be a chemical entity that has not been the subject of an approved NDA in the past. If we receive favorable treatment under the Waxman-Hatch Act for trospium, we may obtain market exclusivity for a period of five years from the date of FDA approval. The marketing of trospium could be materially adversely affected if market exclusivity is not available to us or if the period of market exclusivity is shortened. We expect to seek patent protection for an extended release, once-a-day formulation of trospium. If we were unable to obtain a patent on such formulation we would have to rely solely on market exclusivity for this formulation.

Our products are early stage and may not be successful or achieve market acceptance.

In addition to trospium, we currently have five other compounds which are in various stages of development and have not been approved by the FDA. These product candidates are subject to the risk that any or all of them are found to be ineffective or unsafe, or otherwise may fail to receive necessary regulatory clearances. We are unable to predict whether any of these other product candidates will receive regulatory clearances or be successfully manufactured or marketed. Further, due to the extended testing and regulatory review process required before marketing clearance can be obtained, the time frames for commercialization of any products are long and uncertain. Even if these other product candidates receive regulatory clearance, our products may not achieve or maintain market acceptance.

We rely on the favorable outcome of clinical trials of our product candidates.

Before obtaining regulatory approval for the commercial sale of any of the pharmaceutical products we are developing, we or our licensees must demonstrate that the product is safe and efficacious for use in each target indication. The process of obtaining FDA and other regulatory approvals is lengthy and expensive. If clinical trials do not demonstrate the safety and efficacy of certain products under development, we will be materially adversely affected. The results of pre-clinical studies and early clinical trials may not predict results that will be obtained in large-scale testing or use. Clinical trials of products we are developing may not demonstrate the safety and efficacy of such products. Regardless of clinical trial results, the FDA may not approve marketing of the product. The costs to obtain regulatory approvals could be considerable and the failure to obtain, or delays in obtaining, regulatory approval could have a significant negative effect on our business performance and financial results. Even if pre-market approval of a product is obtained, the FDA is authorized to impose post-marketing requirements. A number of companies in the pharmaceutical industry, including our company, have suffered significant setbacks in advanced clinical trials or have not received FDA approval, even after promising results in earlier trials. For example, while there have been three Phase II clinical trials of pagoclone that demonstrated statistically significant efficacy, two in panic disorder and one in GAD, other trials have failed to demonstrate statistically significant efficacy, prompting Pfizer Inc. (Pfizer) to elect not to pursue further development of the compound and to return to us exclusive, worldwide development and commercialization rights to pagoclone.

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We will rely on third parties to commercialize and manufacture our products.

We do not have necessary sales and marketing capabilities to market our products. Substantial additional funds will be required to complete development and commercialization of our products and, accordingly, we seek corporate partnerships for the manufacture and commercialization of our products. We may not be successful in finding corporate partners and the terms of any such arrangements may not be favorable to us or our security holders. If we are unable to obtain any such corporate partners, development of our product candidates could be delayed or curtailed, which could materially adversely affect our operations and financial condition.

Any collaborative partners may not be successful in commercializing our products or may terminate their collaborative agreements with us. If we obtain any collaborative arrangements, we will depend on the efforts of these collaborative partners and we will have limited or no control over the development, manufacture and commercialization of the products subject to the collaboration. If certain of our collaborative partners terminate the related agreements or fail to develop, manufacture or commercialize products, we would be materially adversely affected. Because we will generally retain a royalty interest in sales of products licensed to third parties, our revenues may be less than if we marketed products directly.

We currently contract with third parties for all of our manufacturing needs and do not manufacture any of our own products or product candidates. Certain of our requirements for supplies or clinical compounds are filled by purchase orders on an as-requested basis and are not the subject of long-term contracts. As a result, we cannot be certain that manufacturing sources will continue to be available or that we can continue to out-source the manufacturing of these products or product candidates on reasonable terms or at all. Any manufacturing facilities for any of our compounds are subject to FDA inspection both before and after NDA approval to determine compliance with U.S. current Good Manufacturing Practices, so-called cGMP , requirements. Facilities used to produce our compounds may not have complied, or may not be able to maintain compliance, with cGMP. The cGMP regulations are complex and failure to be in compliance could lead to non-approval or delayed approval of an NDA. This would delay product launch or, if approval is obtained, may result in remedial action, penalties and delays in production of material acceptable to the FDA.

Our failure to acquire and develop additional product candidates will impair our ability to grow.

We do not conduct our own research to discover new drug compounds. Instead, we depend on the licensing of compounds from others for development. Therefore, in order to grow, we must continue to acquire and develop additional compounds. The success of this strategy depends upon our ability to identify, select and acquire compounds that meet the criteria we have established. Identifying suitable compounds is a lengthy, complex and uncertain process. In addition, we compete with other companies with substantially greater financial, marketing and sales resources, for the acquisition of compounds. We may not be able to acquire the rights to additional compounds on terms we find acceptable or at all.

We need additional funds in the future.

Our existing cash resources together with the proceeds from this offering will be insufficient to commercialize trospium or any of our other product candidates on our own. In addition, we continue to expend substantial funds for product development activities, research and development, pre-clinical and clinical testing, operating expenses, regulatory approval, licensing and other strategic relationships, manufacturing and marketing. In fiscal 2003, net cash used in operating activities was $26,495,000. In the first quarter of fiscal 2004, net cash used in operating activities was $10,900,000. We expect to continue to use substantial cash for operating activities in fiscal 2004 as we continue to fund our development activities, as well as premarketing activities related to trospium. We are seeking a strategic or collaborative partner to

commercialize trospium but may also seek additional funding through other corporate collaborations, strategic combinations or public or private equity and debt financing options. Any such corporate collaboration, strategic combination or financial transactions could result in material changes to the capitalization, operations, management and prospects for our

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business and no assurance can be given that the terms of a strategic transaction would be favorable to us or our security holders. If we raise additional funds by issuing equity securities, existing stockholders will be diluted and future investors may be granted rights superior to those of existing stockholders. There can be no assurance that additional financing will be available on terms acceptable to us or at all. If we sell securities in a private offering, we may have to sell such shares at a discount from the market price of our stock which could have a depressive effect on our stock price.

In addition, future resales of shares in the public market sold in a private offering could negatively affect our stock price. Our cash requirements and cash resources will vary significantly depending upon the following principal factors:

- our ability to receive FDA approval for trospium and successfully commercialize trospium and the nature of any strategic combination, collaboration or funding source regarding the commercialization of trospium;
- the progress of research and development programs;
- costs and results of pre-clinical and clinical testing;
- the timing and cost of obtaining regulatory approvals; and
- whether we are successful in either in-licensing or out-licensing products.

As a result of the uncertainties and costs associated with business development activities, market conditions and other factors generally affecting our ability to raise additional funds, we may not be able to obtain sufficient additional funds to satisfy cash requirements in the future or may be required to obtain financing on terms that are not favorable to us. We may have to curtail our operations or delay development of our products.

We have a history of losses and expect losses to continue.

Other than in fiscal 2000, we have incurred substantial net losses over the past five fiscal years including net losses of approximately $37,800,000, $1,500,000, $17,600,000 and $31,800,000 for fiscal years 1999, 2001, 2002 and 2003 respectively. In the first quarter of fiscal 2004 we incurred a loss of $12,000,000. Through December 31, 2003, we had accumulated net losses since inception of approximately $313,000,000.

We continue to experience losses and to use substantial amounts of cash in operating activities. We will be required to conduct significant development and clinical testing activities for the products we are developing and these activities are expected to result in continued operating losses and use of cash for the foreseeable future. We cannot predict the extent of future losses or the time required to achieve profitability.

We may not be profitable in the future.

We may never achieve or sustain profitability in the future. We expect to continue to experience fluctuations in revenue as a result of the timing of regulatory filings or approvals, product launches, license fees, royalties, product shipments, and milestone payments.

The outcome of the Redux litigation could materially harm us.

On September 15, 1997, we announced a market withdrawal of our first commercial prescription product, the weight loss medication Redux, which had been launched by American Home Products Corp. (AHP), now Wyeth, our licensee, in June 1996. Following the withdrawal, we have been named, together with other pharmaceutical companies, as a defendant in several thousand product liability legal actions, some of which purport to be class actions, in federal and state courts relating to the use of Redux and other weight loss drugs. The existence of such litigation may materially adversely affect our business. In addition, although we are unable to predict the outcome of any such litigation, if successful uninsured or insufficiently insured claims, or if a

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successful indemnification claim, were made against us, our business, financial condition and results of operations could be materially adversely affected. In addition, the uncertainties associated with these legal actions have had, and may continue to have, an adverse effect on the market price of our common stock and on our ability to obtain corporate collaborations or additional financing to satisfy cash requirements, to retain and attract qualified personnel, to develop and commercialize products on a timely and adequate basis, to acquire rights to additional products, and to obtain product liability insurance for other products at costs acceptable to us, or at all, any or all of which may materially adversely affect our business, financial condition and results of operations.

On May 30, 2001, we entered into an indemnity and release agreement with AHP, now Wyeth, which provides for indemnification of Redux-related claims brought by plaintiffs who initially elected not to stay in the AHP national class action settlement of diet drug litigation and by those claimants who allege primary pulmonary hypertension, a serious disease involving the blood vessels in the lungs. This agreement also provides for funding of all defense costs related to all Redux-related claims and provides for Wyeth to fund certain additional insurance coverage to supplement our existing product liability insurance. However, uninsured or insufficiently insured Redux-related claims or Redux-related claims which are not covered by the AHP indemnity and release agreement may arise. Any such claims, if successful, could have a material adverse effect on our business, results of operations and financial condition. We are unable to predict whether the existence of such litigation may adversely affect our business.

We have limited patent protection on some of our products.

Our future success will depend to a significant extent on our ability to:

- obtain and enforce patent protection on our products and technologies;
- maintain trade secrets; and
- operate and commercialize products without infringing on the patents or proprietary rights of others.

Our patents may not afford any competitive advantages and may be challenged or circumvented by third parties. Further, patents may not issue on pending patent applications. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before a potential product can be commercialized, any related patent may expire, or remain in existence for only a short period following commercialization, reducing any advantage of the patent.

Our license for trospium, a compound under development for treatment of overactive bladder, does not include any patents that we expect to use in commercializing the product for overactive bladder.

Our licensed U.S. patent covering the administration of citicoline to treat patients afflicted with conditions associated with the inadequate release of brain acetylcholine has expired. This patent, along with the additional patents issued to us relating to citicoline, may not afford protection against competitors of citicoline to treat ischemic stroke.

Our business may be materially adversely affected if we fail to obtain and retain needed patents, licenses or proprietary information. Others may independently develop similar products. Furthermore, litigation may be necessary:

- to enforce any of our patents;
- to determine the scope and validity of the patent rights of others; or
- in response to legal action against us claiming damages for infringement of patent rights or other proprietary rights or seeking to enjoin commercial activities relating to the affected product or process.

The outcome of any litigation may be uncertain. Any litigation may also result in significant use of management and financial resources.

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To the extent that consultants, key employees or other third parties apply technological information independently developed by them or by others to our proposed products, disputes may arise as to the proprietary rights to such information which may not be resolved in our favor. Most of our consultants are employed by or have consulting agreements with third parties and any inventions discovered by such individuals will not necessarily become our property. There is a risk that other parties may breach confidentiality agreements or that our trade secrets become known or independently discovered by competitors, which could adversely affect us.

We may depend on market exclusivity for certain of our products.

Assuming regulatory approvals are obtained, our ability to commercialize successfully certain drugs may depend on the availability of market exclusivity or patent extension under the Waxman-Hatch Act, which provides protections for certain new products. Under the Waxman-Hatch Act, a company which does not have a patent on a compound may obtain five years of market exclusivity if the FDA determines such compound to be a chemical entity that has not been the subject of an approved NDA in the past. The period of market exclusivity under the Waxman-Hatch Act is considerably shorter than the exclusivity period afforded by patent protection, which, in the case of some patents, may last up to twenty years.

Our products may be unable to compete successfully with other products.

Competition from other pharmaceutical companies is intense and is expected to increase. We are aware of existing products and of products under development by our competitors that address diseases we are targeting and competitors have developed or are developing products or technologies that are, or may compete with our products.

Many of the other companies who market or are expected to market competitive drugs or other products are large, multinational companies who have substantially greater marketing and financial resources and experience than us. We may not be able to develop products that are more effective or achieve greater market acceptance than competitive products. In addition, our competitors may develop products that are safer or more effective or less expensive than those we are developing or that would render our products less competitive or obsolete. As a result, our products may not be able to compete successfully. In addition, royalties payable to us under certain conditions may be reduced or eliminated if there is generic competition.

Many companies in the pharmaceutical industry also have substantially greater experience in undertaking pre-clinical and clinical testing of products, obtaining regulatory approvals and manufacturing and marketing products. In addition to competing with universities and other research institutions in the development of products, technologies and processes, we compete with other companies in acquiring rights and establishing collaborative agreements for the development and commercialization of our products.

We could be materially harmed if our agreements were terminated.

Our agreements with licensors and licensees generally provide the other party with rights to terminate the agreement, in whole or in part, under certain circumstances. Many of our agreements require us to diligently pursue development of the underlying product or risk loss of the license or incur penalties. Depending upon the importance to us of the product that is subject to any such agreement, this could materially adversely affect our business. In particular, termination of our agreement with Madaus, under which we license trospium, or our agreement with Aventis, S.A. (Aventis), under which we license pagoclone, could substantially reduce the likelihood of successful commercialization of our product

candidates which would materially harm us. The agreements with Madaus or Aventis may be terminated by either of them if we are in material breach of our agreements with them or if we become insolvent or file for bankruptcy protection.

We depend upon key personnel and consultants.

We have a small number of employees and are dependent on certain executive officers and scientific personnel, including Glenn L. Cooper, our chief executive officer, Mark S. Butler, our chief administrative

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officer and general counsel, Michael W. Rogers, our chief financial officer and Bobby W. Sandage, Jr., our chief scientific officer. Our business could be adversely affected by the loss of any of these individuals. In addition, we rely on the assistance of independent consultants to design and supervise clinical trials and prepare FDA submissions.

Competition for qualified employees among pharmaceutical and biotechnology companies is intense, and the loss of any qualified employees, or an inability to attract, retain and motivate highly skilled employees, could adversely affect our business and prospects. We may not be able to attract additional qualified employees or retain our existing personnel.

We have product liability exposure and insurance uncertainties related to our products.

The use of products in clinical trials and the marketing of products may expose us to substantial product liability claims and adverse publicity. Certain of our agreements require us to obtain specified levels of insurance coverage, naming the other party as an additional insured. We currently maintain product liability and clinical trial insurance in the amount of $20,000,000. We may obtain additional coverage for products that may be marketed in the future, including trospium. We may not be able to maintain or obtain insurance coverage, or to obtain insurance in amounts sufficient to protect us or other named parties against liability, at a reasonable cost, or at all. In addition, any insurance obtained may not cover any particular liability claim. We have indemnified certain licensors and licensees and may be required to indemnify additional licensors or licensees against product liability claims incurred by them as a result of products we develop or market. If uninsured or insufficiently insured product liability claims arise, or if a successful indemnification claim was made against us, our business and financial condition could be materially adversely affected. In addition, any payments made by us in connection with product liability litigation could result in significant charges to operations and would materially adversely affect our results of operations and financial condition.

Risks Related to Our Common Stock and the Notes

We may issue preferred stock with rights that could affect your rights and prevent a takeover of the business.

Our board of directors has the authority, without further approval of our stockholders, to fix the rights and preferences, and to issue up to 5,000,000 shares of preferred stock, 244,425 of which are currently issued and outstanding. In addition, vesting of shares of our common stock subject to stock awards under our 1997 Equity Incentive Plan accelerates and outstanding options under our stock option plans become immediately exercisable upon certain changes in control of the Company, except under certain conditions. In addition, Delaware corporate law imposes limitations on certain business combinations. These provisions could, under certain circumstances, delay or prevent a change in control of the Company and, accordingly, could adversely affect the price of our common stock. Also, our license agreement for citicoline contains change of control provisions that may have the effect of discouraging or delaying a change of control of the Company.

We have never paid any dividends on our common stock.

We have not paid any cash dividends on our common stock since inception and do not expect to do so in the foreseeable future. Any dividends on our common stock will be subject to the preferential cumulative annual dividend of $0.1253 per share and $1.00 per share payable on our outstanding Series B preferred stock and Series C preferred stock, respectively, held by Wyeth and dividends payable on any other preferred stock we may issue.

If we pay cash dividends on our common stock, you may be deemed to have received a taxable dividend without the receipt of any cash.

If we pay a cash dividend on our common stock which results in an adjustment to the conversion price of the notes, you may be deemed to have received a taxable dividend subject to U.S. federal income tax without the receipt of any cash. See United States Federal Income Tax Consequences Constructive Dividends.

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The price for our securities is volatile.

The market price for our securities and for securities of emerging growth companies have historically been highly volatile. Future announcements concerning us or our competitors may have a significant impact on the market price of our securities. Factors which may affect the market price for our securities include:

- results of clinical studies and regulatory reviews;
- partnerships, corporate collaborations, and strategic corporate transactions;
- announcements by our corporate collaboration partners concerning our products, about which we generally have very limited control, if any, over the timing or content;
- changes in the levels we spend to develop, acquire or license new compounds;
- market conditions in the pharmaceutical and biotechnology industries;
- competitive products;
- sales or the possibility of sales of our common stock or other financings;
- our results of operations and financial condition including variability in quarterly operating results due to timing and recognition of revenue, receipt of licensing, milestone and royalty payments, and regulatory progress and delays;
- proprietary rights;
- Redux-related litigation developments;
- public concern as to the safety or commercial value of our products; and
- general economic conditions.

The high and low sales prices of our common stock as reported by Nasdaq Stock Market were: $6.34 and $5.20 for the first quarter of fiscal 2004, $6.25 and $1.12 for fiscal 1999, $8.75 and $1.34 for fiscal 2000, $10.00 and $1.16 for fiscal 2001, $12.83 and $0.85 for fiscal 2002, and $6.90 and $1.32 for fiscal 2003. Our common stock is subject to delisting if our stock price drops below the bid price of $1.00 per share. If we were to fail to meet any of the continued listing requirements for the Nasdaq Stock Market, our common stock could be delisted from the Nasdaq Stock Market, the effects of which could include limited release of a market price of our common stock and limited news coverage and could result in an adverse effect on the market for our common stock.

The stock markets also experience significant price and volume fluctuation unrelated to the operating performance of particular companies. These market fluctuations may also adversely affect the market price of our common stock.

The price for our common stock could be negatively affected if we issue additional shares or if third parties exercise registration rights.

As of December 31, 2003, we had 47,270,244 shares of common stock outstanding. Substantially all of these shares are eligible for sale without restriction. In addition, Wyeth has the right, under certain circumstances, to require us to register for public sale 622,222 shares of common stock issuable to it upon conversion of the Series B and C preferred stock it owns. We have outstanding registration statements on Form S-3 relating to the resale of our shares of common stock and on Form S-8 relating to shares issuable under our 1989 Stock Option Plan, 1994 Long-Term Incentive Plan, 1995 Employee Stock Purchase Plan, 1997 Equity Incentive Plan, 1998 Employee Stock Option Plan and 2000 Stock Option Plan. We plan to file a Form S-8 to register for resale shares issuable pursuant to our 2004 Equity Incentive Plan. The possibility of sales of such shares, private sales of securities or the possibility of resale of such shares in the public market may adversely affect the market price of our common stock.

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Our stockholders could be diluted if we issue our shares subject to options, warrants, convertible notes, stock awards or other arrangements.

As of March 15, 2004, we had reserved the following shares of our common stock for issuance:

10,817,309